

Utilization of Granulocyte Colony-Stimulating Factor in Non-Small Cell Lung Cancer Patients Receiving Carboplatin-Based Chemotherapy

Authors	Goulnar Kasymjanova, Harvey Kreisman, Esther Dajczman, and David Small
Origin of Study	Canada
Type of Study	SINGLE-CENTER, RETROSPECTIVE COMPARATIVE ANALYSIS BASED ON CHART REVIEW
Objectives	Evaluate the effect of granulocyte colony-stimulating factor (G-CSF, filgrastim) on tumor response and survival of patients with unresectable non-small cell lung cancer
Study Design	The charts of 127 patients treated with carboplatin-based chemotherapy were reviewed for histology, stage, performance status, weight loss, treatment regimen, response, toxicity, and survival. For statistical analysis, Kaplan-Meier methodology and the Cox regression model were used.
Patients	Eighty patients (63%) had stage 3A/3B disease; 47 (37%) were stage 3B (pleural effusion) or stage 4. Eighty-one patients (63%) experienced severe (grade 3/4) neutropenia. Forty-two patients received filgrastim, including 37 patients for severe neutropenia (14 for febrile neutropenia) and 5 patients for active infections during chemotherapy.
Observations	Use of filgrastim had a significant effect on survival (median survival, 21 months vs 15 months for patients who did not receive filgrastim; $P = 0.007$), even though the two patient groups were balanced with respect to disease stage, performance status, weight loss, and dose intensity of chemotherapy. Survival was significantly longer in filgrastim-treated patients than in patients who did not receive filgrastim (20 months vs 15 months; $P = 0.02$), even when survival was measured from the time of starting filgrastim administration. The benefit of filgrastim applied to the subset of patients experiencing severe neutropenia: Median survival was 16 months in 44 severely neutropenic patients who did not receive filgrastim and 21 months in 37 patients with severe neutropenia who received filgrastim ($P = 0.02$). In the Cox regression model analysis, the mortality hazard ratio for patients receiving filgrastim was 0.59 (95% CI: 0.37–0.93; $P = 0.025$). The effect of filgrastim use on survival was confounded by the number of chemotherapy cycles and drug dose intensity; none of the other prognostic factors was significant. A Cox time-dependent model demonstrated that filgrastim had the strongest effect of any variable in the model (hazard ratio, 0.98; $P = 0.039$).
Conclusions	The data suggest that filgrastim may improve survival in patients with advanced non-small cell lung cancer receiving carboplatin-based chemotherapy, an effect that is only partially explained by the time bias due to delay in administration of filgrastim. However, this delay does not account for the entire benefit in patients receiving filgrastim. Prospective studies are required to confirm this finding.
Discussion	Use of filgrastim (Neupogen) may reduce the incidence of febrile neutropenia after chemotherapy and, by preventing neutropenia, may allow for increased dose intensity of chemotherapy. Therefore, the possibility exists that administration of filgrastim may improve survival.

G-CSF Utilization in Non-Small Cell Lung Cancer Patients Receiving Carboplatin-Based Chemotherapy

In this retrospective study of patients with advanced non-small cell lung cancer who received carboplatin-based chemotherapy, investigators found that patients who received filgrastim had improved survival. Multivariate analysis revealed that filgrastim treatment was the only variable that affected survival.

To evaluate the effect of filgrastim on survival and response, investigators reviewed the charts of 127 patients with advanced non-small cell lung cancer (stage 3A/3B, 3B, or 4) who had been treated with carboplatin-based chemotherapy. Investigators collected data on survival, response, treatment regimen, toxicity, stage, histology, performance status, and weight loss.

Of the 127 patients, 81 (63%) had grade 3 or 4 neutropenia, and 42 received filgrastim; this total included 37 administrations of filgrastim for severe neutropenia (14 cases of febrile neutropenia) and 5 for patients with active infections.

Median survival of the filgrastim-treated patients was 21 months, versus 15 months for patients who did not receive filgrastim ($P = 0.007$). This significant effect on survival occurred despite similar patient characteristics between groups, including stage, performance status, and the dose intensity of the chemotherapeutic regimen. Even when measured from the time when filgrastim was first administered, survival was significantly longer in the filgrastim group than among patients who were not treated with the drug (20 vs 15 months, $P = 0.02$).

There was no significant difference in carboplatin dose intensity between the filgrastim and no-filgrastim treatment groups. About half of the filgrastim-treated patients received more than 3 cycles of chemotherapy, compared with 28% of patients in the no-filgrastim group ($P = 0.026$).

The benefit of filgrastim was pronounced in the subset of patients with severe neutropenia. For 44 severely neutropenic patients who did not receive filgrastim, survival was 16 months, compared with 21 months for 37 severely neutropenic patients who did receive filgrastim ($P = 0.02$).

Multivariate analysis showed a mortality hazard ratio of 0.59 (95% CI: 0.37–0.93; $P = 0.025$) for patients who received filgrastim. In a Cox time-dependent model, filgrastim was shown to have the strongest effect of any variable evaluated (hazard ratio, 0.98; 95% CI: 0.96–0.99; $P = 0.039$).

These findings suggest that filgrastim may improve survival in patients with advanced non-small cell lung cancer receiving carboplatin-based chemotherapy. However, the investigators acknowledge that prospective studies would be required to confirm these results.

Key Points

- Filgrastim may improve survival in patients with advanced non-small cell lung cancer receiving carboplatin-based chemotherapy.
- Results of a multivariate analysis performed on the data revealed that the administration of filgrastim was the only variable significantly affecting survival.

References

Kasymjanova G, Kreisman H, Dajczman E, Small D. Utilization of granulocyte stimulating factor (G-CSF) in non-small cell lung cancer (NSCLC) patients receiving carboplatin-based chemotherapy. Poster presented at the 10th World Conference on Lung Cancer; August 10–14, 2003; Vancouver, BC. Abstract P-33.